STATE UNIVERSITY OF NEW YORK
COLLEGE OF MEDICINE AT NEW YORK CITY

TMENT OF MEDICINE

451 CLARKSON AVENUE
BROOKLYN 3, N. Y.

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Dr. Joshua Lederberg
Department of Genetics
University of Wisconsin
Madison, Wisconsin

Dear Joshua:

Your letter of November 20th arrived yesterday and I shall try to answer the queries posed therein. The results of the "crosses" shown in a) and in b) are correct. The usual result of "crossing" DNA from SI-III (which contains genetic units SIII-1 and SI) with cells of the homologous SIII-1 variant is SI-III. As both DNA and cells contain the same SIII-1 unit, SI cells would not be expected to result from such a "cross" unless the SIII-1 unit were deleted from the recipient cells. Such an event does occur infrequently and we have recovered SI cells after the indicated reaction has been allowed to take place, but it is the exception rather than the rule. When one "crosses" DNA from SI-III cells with cells of an heterologous SIII-1 strain (e.g. DNA SIII-1-I-III with SIII-1c cells) the results are more complicated.

The recipient cells in reaction b) are equivalent to Harriet's R36A strain. The strain we use is R36NC and both were derived originally from the capsulated type II strain, D39S.

I have never been too happy about assessing results of capsular transformation reactions with regard to cell types for which no selective technique for isolation exists. We have tried to detect non-capsulated cells by crossing DNA from R36A or R36 NC with cells of SIII-1 and studying 50 or 100 clones isolated following this reaction but we have never come up with one. There may be a difference, however, in the mechanism of intratype and intertype transformations. When DNA SIII-1-I-III is crossed with cells of SIII-1c, for example, SIII-N is the most common result of such a reaction. In the absence of really satisfactory quantitative methods, however, I am inclined to be very guarded indeed about drawing conclusions from experiments concerned with capsular factors.

At the moment, our great problem is finding a satisfactory symbolic nomenclature for dealing with these strains. We have been using a mixed genotypic-phenotypic formula which leaves much to be desired: i.e., strain SIII-1c-I-III is a strain containing genetic units SIII-1c and SI and expressing phenotypes SI and SIII-N. If you have any suggestions to make about this problem, I

should welcome them. Terminology is, at the moment, a major impediment to publication of the considerable data we have accumulated.

Thanks in advance for any ideas you may have.

Sincerely,

Bob

Robert Austrian, M.D.

RA/hlr

SOME BIOLOGIC PROPERTIES OF DOUBLY ENCAPSULATED PNEUMOCOCCI

Robert Austrian* and Harriet P. Bernheimer, New York, N.Y.

From pneumococcal transformation reactions, doubly encapsulated organisms forming simultaneously polysaccharides types I and III or types III and V have been isolated. These cellular types result from the interaction of desoxyribonucleates from pneumococci of type I or type V with the cells of a pneumococcus derived from capsular type III. In each instance, the introduction of the genetic unit for the production of a new capsular polysaccharide into cells of the strain derived from type III is followed by a significant increase in the production of type III polysaccharide as well as by the formation of polysaccharide of a different serologic type.

Cells of doubly encapsulated variants give a positive quellung reaction with type specific antiserum against each of their capsular components. Exposure to the soil bacillus enzyme which specifically hydrolyzes type III polysaccharide results in loss by the cell of the positive quellung reaction with type III antiserum, but reactivity with the antiserum to the second capsular polysaccharide is retained. When doubly encapsulated strains are grown in the presence of antiserum against either capsular component, the cells are agglutinated. In mice, both varieties of doubly encapsulated pneumococci are highly virulent. Mice can be protected against a hundred lethal infecting doses of such organisms, however, by antiserum against either of their capsular components. Such protection is not afforded by a single antiserum when infection is induced with mixtures of two pneumococcal strains each producing but one of the capsular polysaccharides of the doubly encapsulated variant.

The experiments provide another basis for explaining serologic cross reactions in pneumococcus and demonstrate that antigen-antibody reactions involving either of two surface components of the cell may result in protection against lethal infection.

J. Cl. Dausch.